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EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
09/18/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/531,701	ROUGON ET AL.	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *1-11,18 and 21-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-15,19,20,24 and 25* is/are rejected.

7)☒ Claim(s) *16 and 17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948).
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restriction file on July 27, 2007 is acknowledged. Claims 1-28 are pending in this application.

Restriction

1. Applicant's election with traverse of Group 95 (claims 12-17, 20 and 24-25) in the reply filed on July 27, 2007 is acknowledged. The traversal is on the ground(s) that Groups 1 to 105 have unity of invention and therefore, are improperly restricted. The peptides in these groups have, for example, both structural and functional features. The Applicant argues that a functional feature for example, is a B epitope of a PSA attached to a NCAM that is recognized by an anti-PSA antibody. The Applicant argues that a structural feature for example is a peptide conformation representing the B epitope of a PSA attached to NCAM. Further, the Applicant argues that unity of invention restrictions are not justified for the dependent claims because unity of invention applies only in relation to independent claims and not to dependent claims. This is not found persuasive because the peptide sequences claimed are patentably independent and distinct due to the amino acid content leading to different structures. For example, DSPLVPRIDFHP (SEQ ID NO: 1) is not the same as SDQGVNGSWSNP (SEQ ID NO: 11) or CWPLGDSTVICG (SEQ ID NO: 24) and does not share any common core sequence. Furthermore, a linear peptide is not the same as a cyclic peptide, structurally and in sequence. As recited in the previous office action, When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being a similar nature

where the following criteria are fulfilled: (A) All alternatives have a common property or activity; and (B)(1) A common structure is present, i.e., a significant structural element is shared by all of the alternatives (see PCT RULE 13.2). This would require independent searches, leading to burdensome search on the Examiner. Furthermore, the search for each of the inventions is not co-extensive particularly with regard to the literature search. Burden consists not only of specific searching of classes and subclasses, but also of searching multiple databases for foreign references and literature searches. Burden also resides in the examination of independent claim sets for clarity, enablement, and double patenting issues. Further, a reference that would anticipate the invention of one group would not necessarily anticipate or even make obvious another group. Finally, the consideration for patentability is different in each case. Thus, it would be an undue burden to examine all of the above inventions in one application and the restriction for examination purposes as indicated above is deemed proper.

2. In regards to the argument that unity of invention restrictions are not justified, claims 1-2 and 9-11 link(s) inventions 1 through 54 (those claims that are dependent claims). In linking claims practice, the restriction requirement among the linked inventions is subject to nonallowance of the linking claim(s). Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104. Thus, the restriction requirement of

dependent claims is justifiable. Thus, restriction for examination purposes as indicated above is deemed proper.

3. The requirement is still deemed proper and is therefore made FINAL. Claims 1-11, 18, 21-23, 26-28 are withdrawn from further consideration, pursuant to 37 CFR 1.142(b), as being drawn to nonelected Inventions, there being no allowable generic or linking claim. Claim 19 was inadvertently omitted from the restriction practice. Thus, claim 19 is being grouped together with Group 95. Please also note that Groups 55-103 follow a linking claim practice. The Group Restriction is as follows for Groups 55-103:

Groups 55-78, claim(s) 16, drawn to a medicament and a pharmaceutical composition comprising a linear peptide comprising an amino acid sequence SEQ ID NOs: 1-12 and 14-26, respectively (i.e., Group 55=SEQ ID NO: 1, Group 78=SEQ ID NO: 26, etc).

Groups 79-103, claim(s) 16, drawn to a medicament and a pharmaceutical composition comprising a cyclic peptide comprising an amino acid sequence SEQ ID NOs: 1-12 and 14-26, respectively (i.e., Group 79=SEQ ID NO:1 , Group 103=SEQ ID NO: 26, etc).

Thus, claims 12-15, 17-20 and 24-25 link(s) inventions 55 through 78. The restriction requirement among the linked inventions is **subject to** the nonallowance of the linking claim(s), claim 12-15, 17-20 and 24-25. Claims 12-15, 17, 19-20 and 24-25 link(s) inventions 79 through 103. The restriction requirement among the linked inventions is **subject to** the nonallowance of the linking claim(s), claim 12-15, 17, 19-20 and 24-25. Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions **shall** be withdrawn and any claim(s) depending from or

otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 **Claims that require all the limitations of an allowable linking claim** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

4. Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01. A search was conducted on the elected invention, SEQ ID NO: 18, and this is deemed free of prior art. The search was extended to the broad generic claim 14 (or claim 1 pertaining to product only), and prior art was found. Claims 1 and 9 have been examined only as limitation of the product claims 12-17, 19-20 and 24-25. Claims 12-17, 19-20 and 24-25 are examined on the merits in this office action.

Objection-Claim

5. Claim 19 is objected to for the following informality: The claim recites " the peptide...wherein the is a cyclic peptide". The recitation appears to have an error. The

limitation should read, "The peptide...wherein the cyclic peptide in...". The Applicants are advised to correct this error.

Rejection-35 U.S.C. 112, 2nd

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 1 and 14 recite the broad recitation "a peptide consisting of 5 to 30 amino acids" and the claim also recites "preferably 9 to 15, most preferably about 12 amino acid residues" which is the narrower statement of the range/limitation. Please note that claim 1 was only examined on the limitation of the peptide composition.

8. Claim 19 recites "The peptide according to claim 17, wherein the cyclic peptide in which the side chain of the cysteine residue at position 1 of SEQ ID NO: 18 or SEQ ID NO: 22 is attached covalently to the side chain residue of the cysteine at position of 11 of SEQ ID NO: 18 or SEQ ID NO: 22 via a disulfide bond". This recitation is unclear. It is unclear if position 1 of SEQ ID NO: 18 is attached to the position 11 of SEQ ID NO: 18 or position of 11 of SEQ ID NO: 22 OR position 1 of SEQ ID NO: 22 is attached to position 11 of SEQ ID NO: 18 or position o11 of SEQ ID NO: 22.

Rejection-35 U.S.C. 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Rao et al (Journal of Cell Biology, 1992, 118(4): 937-949) as evidence by Storms et al (J. Biol., Chem., 1998, 273(4): 27124-27129).

11. The instant claim is drawn to a peptide (linear or cyclic) consisting of 5 to 30 amino acids, the peptide comprising a B epitope of a poly-α2,8 sialic acid (PSA) attached to NCAM, which is recognized by anti-PAS antibody.

12. Rao et al teach that NCAM is diversified by posttranslational modification, α-2,8-linked polysialic acid (see p. 937, right column, 1st paragraph). Furthermore, the

reference indicates that NCAM appears to participate in cell-cell adhesion via homophilic interaction (see p. 937, right column, 2nd paragraph). As evidenced by Storms et al, the polysialic acid (PSA) moiety of NCAM can serve as a negative regulator of homophilic binding (see abstract). Rao et al further discloses that to more define NCAM homophilic binding sites, they have used three different strategies, including analysis of domain deletion mutants, mapping of mAb epitopes, and use of synthetic oligopeptides to inhibit NCAM homophilic interaction. A sequence of 10 amino acids (KYSFNYDGSE) located in domain 3 is directly involved in NCAM homophilic binding (see p. 938, left column, 1st paragraph). Since PSA is a naturally occurring moiety of the NCAM, it would inherently have peptide comprising the B epitope of PSA, and this would be recognized by anti-PSA. Furthermore, since the reference discloses the epitope mapping to the homophilic site, this meets the limitation of claim 14. Furthermore, the reference discloses a 21mer (P5), a 10mer (P10), and 14mer (P3) that show inhibition of NCAM cell aggregation and vesicle adhesion (see Tables III, IV and V). Table IV further shows the combination of P3 and P10 peptides to see if the two peptides would have any additive effect (no additive effect seen). The reference reads on claims 14 and 15.

Rejection-35 U.S.C. 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 12-13, 20 and 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rao et al (Journal of Cell Biology, 1992, 118(4): 937-949) as evidence by Storms et al (J. Biol., Chem., 1998, 273(4): 27124-27129) as applied to claims 14-15 above, and further in view of Blaschuk et al (US Patent # 6346512).

17. The instant claims are drawn to a medicament and a pharmaceutical composition consisting of a peptide of 5 to 30 amino acids and comprising optionally in combination with a pharmaceutically acceptable carrier. The claims are further drawn to a peptide

complex wherein the peptide comprises several identical or different peptides linked by covalent or non-covalent bonds.

18. As describe supra, Rao et al teach . A sequence of 10 amino acids (KYSFNYDGSE) located in domain 3 is directly involved in NCAM homophilic binding (see p. 938, left column, 1st paragraph). Since PSA is a naturally occurring moiety of the NCAM, it would inherently have peptide comprising the B epitope of PSA, and this would be recognized by anti-PSA. Furthermore, since the reference discloses the epitope mapping to the homophilic site, this meets the limitation of claim 14. Furthermore, the reference discloses a 21mer (P5), a 10mer (P10), and 14mer (P3) that show inhibition of NCAM cell aggregation and vesicle adhesion (see Tables III, IV and V). Table IV further shows the combination of P3 and P10 peptides to see if the two peptides would have any additive effect (no additive effect seen). This reads on claims 14-15. The difference between the reference and the instant claims are that the reference does not teach a medicament or a pharmaceutical composition and the covalent or non-covalent bond linkage of peptides.

19. However, Blaschuk et al teach cyclic peptides and compositions comprising such cyclic peptides that comprise a cadherin cell adhesion recognition sequence HAV (see abstract). The reference further teaches that multiple CAR (cell adhesion recognition) sequences may be present within a modulating agent, and CAR sequences that may be included within a modulating agent are any sequences specifically bound by an adhesion molecule...preferred CAR sequences for inclusion within a modulating agent include RGD...KYSFNYDGSE (SEQ ID NO: 53), which is bound by N-CAM...(see

column 11, lines 24-45). Furthermore, the reference teaches that linkers may be used to separate CAR sequences and/or antibody sequences within a modulating agents...a linker may be any molecule (including peptide and/or non-peptide sequences) that does not contain a CAR sequence and that can be covalently linked to at least two peptide sequences. Using a linker, HAV-containing cyclic peptide and other peptide or protein sequence may be joined head-to-tail, head-to-side chain and/or tail-to-side chain (see column 12, lines 17-29). Furthermore, the reference teaches that the composition comprising a cell adhesion modulating agent is provided as a pharmaceutical composition in combination with a pharmaceutically acceptable carrier (see column 3, lines 48-51). The reference further discloses that the fluid compositions typically contain about 10 ng/ml to 5 mg/ml, preferably from about 10 μg to 2 mg/ml cyclic peptide (see column 26, lines 48-50). The instant specification discloses that the effective peptide in the composition is in a concentration ranges from about 0.1 μM to about 10 μM (see paragraph [0061]).

20. Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Rao and Blaschuk et al, since they both teach the sequence KYSFNYDGSE (NCAM bound peptide) in a composition for modulating of cell adhesion. There is a reasonable expectation of success since Rao et al teach that the peptide sequence site is directly involved in NCAM homophilic interaction, and that Blaschuk et al teach that SEQ ID NO: 53 is bound by N-CAM, thus it is well known that that peptide sequence is at the site of PSA, and the anti-PSA would recognize and bind to the peptide sequence. Furthermore, Blaschuk et al teach that the cadherin-mediated cyclic

peptide can be covalently linked to other non CAR peptides in pharmaceutical composition.

21. Furthermore, It has been held that under KSR that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in KSR, When there is motivation "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727,_,82 USPQ2d 1385, 1397 (2007).

22. The "problem" facing those in the art was identifying to regions of NCAM that participates directly in NCAM-NCAM binding, modulating cell adhesion for inhibiting abnormal cellular adhesions, and modulating cell adhesion for allowing permeability for the delivery of drugs to specific tissues and tumors within the body, and there were a limited number of methodologies available to do so, for example specific receptors or carrier proteins that transport molecules across barriers in vivo. However, due to the low endogenous transport rates or to the poor functioning of a carrier protein with drugs, these receptors and carrier proteins were often inefficient. The skilled artisan would have had reason to try these methodologies with the reasonable expectation that at least one would be successful. In this case, because the 10mer, 21mer disclosed in Rao et al were effective in inhibiting membrane vesicle adhesion and cell aggregation and Blaschuk et al disclosed that 10mer disclosed in Rao et al could be used in

combination with CAR and other peptides to form a pharmaceutical composition. Thus, formulating a peptide composition consisting of 5 to 30 amino acids, comprising a peptide of a PSA attached to NCAM which is recognized by anti-PSA covalently or non-covalently bonded to another cell adhesion molecule such as cadherin cell adhesion molecule (found in neural cells, endothelial cells and a variety of cancer cell types) (see Blaschuk, column 1, lines 61-63) is a "the product not of innovation but of ordinary skill and common sense," leading to the conclusion that invention is not patentable as it would have been obvious.

Conclusion

Allowable Subject Matter

23. Claims 16 and 17 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Please note that only the elected Group drawn to cyclic peptide sequence CSSVTAWTTGCG (SEQ ID NO: 18) have been examined. Claims drawn to SEQ ID NOs: 1-12, 14-17 and 19-26 have not been examined, since they belong to nonelected inventions, Groups 55-78, 79-94 and 96-103, as well as Groups 1-54 and 104-105.

24. Claims 12-15, 19-20, and 24-25 have been rejected. No claims are allowed.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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9/4/08
ANISH GUPTA
PRIMARY EXAMINER